TITLE: VA Central Institutional Review Board (IRB) Authority, Responsibilities, and Activities

1.0 PURPOSE

This Standard Operating Procedure (SOP) sets forth the authority and responsibilities of the VA Central Institutional Review Board (IRB). It also contains procedures for identifying and reporting undue influence on the VA Central IRB or any of its members.

2.0 REVISION HISTORY

Date of Initial Approval	June 6, 2008
Revision Dates	September 23, 2009 March 30, 2010

3.0 SCOPE

This SOP applies to all research that is submitted to the VA Central IRB for review. It pertains to investigators, VA Central IRB members and administrative staff, VA Central IRB administrative staff, and local VA facilities that have entered into a Memorandum of Understanding (MOU) with the Veterans Health Administration Central Office (VHACO) Human Research Protections Program (HRPP) listing the VA Central IRB as an IRB of record for their facility.

4.0 POLICY

4.1 It is the policy of the VHACO HRPP that the VA Central IRB operates as an independent authority to carry out all the responsibilities required of an IRB in accordance with VA and other requirements, and that any attempt to exert undue influence on the VA Central IRB or any VA Central IRB member individually is promptly identified and reported (see paragraph 7.9.1.)

4.2 It is the policy of the VHACO HRPP that the VA Central IRB oversees human participant research designated for review by the VA Office of Research and Development (ORD). ORD designated research is submitted to the VA Central IRB by investigators from VA facilities that have an MOU with the VHACO HRPP to serve as an IRB of record. The VA Central IRB may not oversee research for any VA facility until that facility has listed the VA Central IRB on its FWA and entered into an MOU with VHACO. Commercial IRBs are not used for approval of VA research.

5.0 DEFINITIONS

See VA Central IRB SOP 128, Definitions Used in VA Central IRB SOPs.

6.0 RESPONSIBILITIES

6.1 Institutional Official – See SOP VA Central IRB SOP 100, Veterans Health Administration Central Office (VHACO) Human Research Protection Program (HRPP) Overview, Structure, and Responsibilities.

6.2 Chief Research and Development Officer (CRADO) – See SOP VA Central IRB SOP 100, Veterans Health Administration Central Office (VHACO) Human Research Protection Program (HRPP) Overview, Structure, and Responsibilities.

6.3 Director, Program for Research Integrity Development and Education (PRIDE) – See SOP VA Central IRB SOP 100, Veterans Health Administration Central Office (VHACO) Human Research Protection Program (HRPP) Overview, Structure, and Responsibilities.

6.4 Local VA Facility IO – The local facility IO is the Signatory Official for the institution when entering into an MOU with the VHACO HRPP designating the VA Central IRB as an IRB of record on its FWA. The local facility IO is responsible for ensuring that the facility meets all the obligations as set forth in the MOU and that no research submitted to the VA Central IRB is otherwise approved or begun at the facility until it is approved by both the VA Central IRB and in accordance with VHA Handbook 1200.01. In VA facilities, the IO is the Medical Center Director.

6.5 VA Central IRB – The VA Central IRB is responsible for fulfilling all responsibilities and for performing all functions of an IRB in accordance with 38 CFR 16 and VHA Handbook 1200.05, including but not limited to the authority to:

6.5.1 Approve, require modifications to secure approval, or disapprove research activities brought before it in order to assure the rights and welfare of human research participants are being protected.

6.5.2 Suspend or terminate approval of research not being conducted in accordance with the VA Central IRB's requirements or due to concerns regarding the safety, rights, or welfare of human research participants, research project staff, or others.

6.5.3 Observe or have a third party observe, the informed consent process and the conduct of the research.

6.6 VA Central IRB Administrator – The VA Central IRB administrator is responsible for overseeing the daily administrative activities of the VA Central IRB. This includes ensuring that all local VA sites participating in a VA-funded, multi-site project submitted to the VA Central IRB for review, have an approved MOU on file and that the VA Central IRB has been designated as an IRB of record on the local site's FWA. If the site does not have an approved MOU in place, and/or is not designated as an IRB of record on the facility's FWA, the VA Central IRB Administrator works with the local

facilities in submitting and processing these documents. The VA Central IRB Administrator also maintains a database of all local VA facilities with approved MOUs and their renewal dates.

6.7 VA Central IRB Coordinators – The VA Central IRB Coordinators are responsible for the daily activities of the VA Central IRB including but not limited to coordinating all project review functions of the VA Central IRB with the designated VA Central IRB reviewers, the VA Central IRB Co-Chairs, and the study teams in accordance with established policies and procedures. The VA Central IRB Coordinators maintain all required documentation, including but not limited to a record of all actions taken by the VA Central IRB in regard to their assigned projects.

7.0 PROCEDURES

7.1 Review of Research. All research involving human participants submitted to the VA Central IRB, whether an initial or continuing review, will be reviewed either at a meeting of the convened IRB or through expedited review procedures, unless it meets the criteria for exempt research.

7.1.1 Research meeting the criteria for exempt research will be reviewed and documented in accordance with VA Central IRB SOP 107, Request for Exemption Review and Determination.

7.1.2 Except where an expedited review procedure is used, the VA Central IRB reviews proposed research at convened meetings where a quorum is present, including at least one voting member whose primary concern is in a non-scientific area and one voting member whose primary concern is in a scientific area. If the research is FDA-regulated, a voting licensed physician member is included in the quorum.

7.2 Review Requirements. In conducting the review, the VA Central IRB determines that all of the following requirements are satisfied in accordance with 38 CFR 16 and VHA Handbook 1200.05:

7.2.1 Risks, both physical and non-physical, to human participants are minimized by using procedures that are consistent with sound research design; that do not unnecessarily expose participants to risk; and, whenever appropriate, using procedures already being performed on the participants for diagnostic or treatment purposes.

7.2.2 Risks, both physical and non-physical, to human participants are reasonable in relation to any anticipated benefits to participants (the risk/benefit ratio), and the importance of the knowledge that may reasonably be expected to result. Validity of research design is taken into consideration in determining the risk/benefit ratio.

7.2.3 The selection of participants is equitable for the purposes of the research and the research setting. The VA Central IRB is particularly cognizant of the special issues of research involving vulnerable populations such as children, prisoners, pregnant women, or persons with impaired decision-making capability, as well as special classes of participants such as economically or educationally disadvantaged individuals, and will determine if additional safeguards are required for these populations in the projects reviewed.

7.2.4 Informed consent will be sought for each prospective participant, or the participant's legally authorized representative, and a written, informed consent document is included as part of the research project, if applicable.

7.2.4.1 The wording of the informed consent form includes all required elements, and any additional elements as applicable, per 38 CFR 116 and in accordance with VHA Handbook 1200.05.

7.2.4.2 The VA required language for a valid authorization to release Protected Health Information under the Health Insurance Portability and Accountability Act (HIPAA) is included as a separate document. The VA Central IRB may waive the requirement for an authorization or may alter the authorization only in accordance with VHA Handbook 1605.1, Privacy and Release of Information.

7.2.5 Documentation of the informed consent process itself is included in the research project. It is the responsibility of the VA Central IRB to ensure that the proposed project contains documentation concerning how informed consent will be sought from each participant or their legally authorized representative, and that only a person knowledgeable about the consenting process and the research conducted obtains the informed consent.

7.2.6 When appropriate, the project plan makes adequate provisions for monitoring the data collected to ensure the safety of participants. The VA Central IRB reviews the data safety and monitoring plan to ensure adequate protections have been included for participant populations.

7.2.7 Adequate provisions are included in the project to protect the privacy of participants and to maintain the confidentiality of individually identifiable data. The requirements of the HIPAA Privacy Rule and other federal requirements regarding the protection and use of Veterans' information should be considered in the provisions.

7.2.8 Additional safeguards are included in each project, if applicable, to protect the welfare of vulnerable participants or other special classes of participants who may be vulnerable to coercion or undue influence.

7.2.9 Steps to manage, reduce, or eliminate potential or real conflicts of interest (financial, professional or personal role relationships, and/or institutional) have been taken.

7.2.10 The Principal Investigator/Study Chair (PI/SC) and all other investigators that will be involved in the proposed project have met all current educational requirements for the protection of human research participants as mandated by the facility's assurance and VA policy.

7.3 Actions Taken by the VA Central IRB. The VA Central IRB notifies the PI/SC and the local VA facilities participating in the project in writing of its decision to approve or disapprove a project activity, or of modifications required to secure approval.

7.3.1 Prior to issuing an approval letter, the VA Central IRB ensures that all the requirements of 38 CFR 16.111 and 38 CFR 16.116 and 117 as applicable and detailed in paragraph 7.2 have been met.

7.3.2 If modifications are required to secure approval, these are detailed in the letter to the investigator. The following additional review by the VA Central IRB is then required depending upon the type of modification that was requested and the review that was conducted:

7.3.2.1 If the convened VA Central IRB requires substantive modifications or clarifications to the project and/or informed consent, the convened VA Central IRB must review and approve all materials submitted by the PI in response before an approval letter can be issued.

7.3.2.2 If the convened VA Central IRB requires minor modifications in a project, one of the VA Central IRB Co-Chairs or another qualified voting member designated by the Co-Chair, may review the PI/SC's response and, using an expedited review procedure, approve the revised research project on behalf of the VA Central IRB.

7.3.2.3 If modifications are required during the expedited review process, these modifications will be reviewed by the original reviewer and the Co-Chair prior to an approval letter being issued.

7.3.3 If the VA Central IRB disapproves a project, a written statement detailing the reasons for its decision is sent to the PI/SC, giving the PI/SC an opportunity to respond in writing. If the PI/SC wishes to respond to the VA Central IRB decision in person, the PI/SC will be invited to present the response at a convened meeting. If a project is disapproved by the VA Central IRB, the decision cannot be overruled by a higher authority or a participating facility.

7.4 Required Written Procedures. The VA Central IRB establishes written procedures for, but not limited to the following:

7.4.1 Conducting initial and continuing review of research and for reporting the VA Central IRB's findings to the investigator and appropriate local VA participating facility institutional officials as designated per the MOU.

7.4.2 Determining which projects require review more than annually and which projects require verification from sources other than the investigator that no material changes have occurred since the previous review.

7.4.3 Requiring that investigators promptly report proposed changes in a research project to the VA Central IRB, including amendments to a project, to include the consent form, and for ensuring that such changes in approved projects are not initiated without the VA Central IRB's review and approval, except when necessary to eliminate apparent immediate hazard to the participants.

7.4.4 Requiring prompt reporting of non-compliance by project personnel to the VA Central IRB.

7.4.5 Reporting of any unanticipated adverse events and/or unanticipated problems as required by VA and other federal requirements to the VA Central IRB and for notifying appropriate oversight authorities of any adverse events or unanticipated problems that cause harm or risk of harm to human participants in accordance with VHA Handbook 1058.01.

7.4.6 Terminating or suspending VA Central IRB approval of a research project.

7.4.7 Observing the informed consent process when the VA Central IRB determines it to be appropriate.

7.4.8 Conducting audits of projects and other VA Central IRB activities.

7.4.9 Ensuring that initial and continuing educational requirements for the VA Central IRB Co-Chairs and members are met.

7.4.10 Reporting to the VHA Privacy Officer and coordinating with local VA facilities for local reporting of any unauthorized use, loss, or disclosure of individually identifiable patient information, and for reporting violations of VA information security requirements to the appropriate VHA Information Security Officers within one hour.

7.5 Ongoing Monitoring.

7.5.1 The VA Central IRB has the authority to conduct audits of pertinent local VA facility files to ensure all written procedures are followed and to review research records and research case histories for compliance with written procedures and other requirements. This includes monitoring the informed consent process and the research or having a designated third party perform the monitoring.

7.5.2 The VA Central IRB may also review the results of audits conducted by other entities.

7.6 Continuing Review.

7.6.1 The VA Central IRB conducts continuing review of research at intervals appropriate to the degree of risk, but not less than once per year. In the continuing review, the VA Central IRB determines that all the requirements detailed in paragraph 7.2 of this SOP are satisfied.

7.6.2 If the research does not occur within the timeframe set by the VA Central IRB, the VA Central IRB approval automatically lapses. See VA Central IRB SOP 112, Continuing Review and Approval Requirements for Investigators, for further information on lapsed approvals.

7.7 Maintenance of Documentation: The VA Central IRB prepares and maintains complete documentation of its activities to include the following:

- Current status of FWA and IRB Registration
- Current MOUs
- VA Central IRB roster and member qualifications
- Minutes of the meetings
- Copies of all items reviewed as part of the project file
- Copies of all project determinations made by the VA Central IRB
- Records of continuing review
- Statements of significant new findings provided to participants
- Copies of all correspondence between the investigators and the VA Central IRB and between the participating sites and the VA Central IRB
- Reports of serious adverse events, complaints, unanticipated problems involving risks to subjects or others, and reports of non-compliance as well as all actions taken by the VA Central IRB in response or connection to these reports

7.8 Serving as an IRB of Record.

7.8.1 When the VA Central IRB serves as an IRB of record for a participating site in a multi-site project, it has the authority and responsibilities detailed in paragraphs 7.1 through 7.7 of this SOP. Additionally, the VA Central IRB adheres to all duties and responsibilities as detailed in the attached MOU.

7.8.1.1 In review of the research as it will be conducted at the local participating site, the VA Central IRB evaluates the local site resources, qualifications of the investigators, and any other local context issues such as the characteristics of the site's patient population; and determines that the site is capable of carrying out the proposed research.

7.8.1.2 Each site having its own FWA enters into an MOU with the VA Central IRB, irrespective of other IRB arrangements.

7.8.2 If an MOU is not in place, the local facility follows these procedures to establish an MOU with the VA Central IRB.

7.8.2.1. The local facility submits a completed MOU based on the approved template for signature to the local facility IO and the applicable VA Integrated Service Network (VISN) Director. They also add the VA Central IRB as an IRB of record to the facility FWA. VA Central IRB administrative staff will assist the local facility in providing all the required information concerning the VA Central IRB in order for the amended FWA, revised VA FWA addendum, and MOU to be prepared.

7.8.2.2. The local VA facility notifies ORO when the amended FWA and the revised VA FWA addendum are ready for review. ORO electronically reviews the revisions and notifies the facility when to submit the revisions to OHRP. The local VA facility then submits a signed hard copy of the FWA and the VA addendum to ORO.

7.8.2.3 The local VA facility submits the signed copy of the MOU to the VA Central IRB Administrative Office. Personnel in the VA Central IRB Administrative Office obtain the signature of the IO or designee on behalf of the VHACO HRPP and forward a signed copy to both the local VA facility and to ORO.

7.8.3 No research may be reviewed by the VA Central IRB as an IRB of Record from a site until the site's amended FWA is approved by ORO and OHRP and is posted on the OHRP website listing the VA Central IRB as an IRB of record for that site and a signed MOU with the site is on file.

7.8.4 The MOU with each site will be reviewed and updated as necessary.

7.8.4.1 The MOU must be renewed every three years or earlier if there is a change in a local facility IO. Upon receipt of a notice from OHRP of a change in Signatory Official on the FWA for a site that lists the VA Central IRB as an IRB of record, the site is contacted and asked to submit an updated MOU with the current IO's signature within 30 days.

7.8.4.2 If there is a change in the HPA or if there is an update in the current IO information, such as changing an "Acting Director" title to a "Director" title the MOU need not be re-submitted. If the change pertains to updating the current IO information, a letter from the facility on its letterhead indicating the change in title is requested from the local facility and appended to the current MOU upon receipt.

7.8.5 The SOPs for the VA Central IRB are posted on the VA Central IRB website to facilitate access by participating sites in order for them to update local site SOPs to incorporate the policies and procedures of the VA Central IRB.

7.9 Independence of VA Central IRB. The VA Central IRB is an independent authority. The Co-Chairs and individual members are recruited from throughout the nation. Its structure and oversight mechanisms have been developed to minimize the

possibility of any Institutional COI or undue influence. However, in the event that an investigator, VA Central IRB member, human research participant, or any other interested party believes there has been an attempt to unduly influence the VA Central IRB or one of its members, the following actions should be taken:

7.9.1 Anyone who wishes to report what they believe is an attempt to unduly influence the VA Central IRB or one of its members can report such an attempt to one or more of the following entities:

- VA Central IRB Co-Chair
- VA Central IRB Administrator
- VA Central IRB Coordinator
- The Director, PRIDE
- The CRADO (HPA for VHA Central Office HRPP)
- The Principal Deputy Under Secretary for Health (IO for the VHA Central Office HRPP)

7.9.2 Upon receipt of a report to unduly influence the VA Central IRB or one of its members, the individual receiving the report immediately informs the IO of the VHACO HRPP. The IO will appoint an individual or individuals to investigate the allegations and prepare a report of findings.

7.9.3 Depending upon the allegations and the outcome of the investigation, the VA Central IRB or IO as applicable may take one or more of the following actions:

- Barring an investigator from submitting any further research to the VA Central IRB
- Suspending or terminating any currently approved research projects pertaining to the allegations in accordance with approved procedures
- Terminating the membership of any VA Central IRB members involved

7.9.4 Other administrative or disciplinary actions may be taken by the appropriate supervisory authorities as applicable depending upon the results of the investigation.

8.0 REFERENCES

8.1 38 CFR 16, Department of Veterans Affairs, Protection of Human Subjects

8.2 VHA Handbook 1200.01, Research and Development Committee

8.3 VHA Handbook 1200.05, Requirements for the Protection of Human Subjects in Research

8.4 VHA Handbook 1058.03, Assurance of Protection from Human Subjects in Research

8.5 VHA Handbook 1605.1, Privacy and Release of Information

8.6 21 CFR 56, U.S. Food and Drug Administration, Institutional Review Board

8.7 45 CFR 164.508, HIPAA Privacy Rule

8.8 MOU checklists developed by ORO and ORD

Attachment
MOU Template

I have reviewed and approved the contents of this SOP.

K. Lynn Cates, MD
Director, PRIDE

Date: 4/2/2010

Memorandum of Understanding

VA Central IRB
VA Institutional Review Board for Multisite Studies

MEMORANDUM OF UNDERSTANDING

BETWEEN
VETERANS HEALTH ADMINISTRATION (VHA)
CENTRAL OFFICE

AND

{NAME OF LOCAL VETERANS AFFAIRS (VA) FACILITY}

PURPOSE

1. This Memorandum of Understanding (MOU) sets forth the agreed upon respective authorities, roles, and responsibilities of the Veterans Health Administration (VHA) Central Office, operating VA Central Office Institutional Review Board (IRB), hereinafter referred to as VA Central IRB, and the {Name of Local VA Facility}, for the initial and continuing review, as well as review of amendments, monitoring, reporting, and other relevant requirements, for select multi-site research projects involving human subjects.

2. This MOU does not preclude {Name of Local VA Facility} from continuing to participate in any existing agreements the {Name of Local VA Facility} may have with other VA or non-VA entities. This MOU is between the signatories only and does not include any other entities that are independently operating under their own Federalwide Assurances (FWAs), and it specifically excludes other entities with which {Name of Local VA Facility} may have a separate MOU for IRB and/or Research and Development (R&D) Committee services.

GENERAL PROVISIONS

1. Both signatory institutions will be guided by the "Ethical Principles and Guidelines for the Protection of Human Subjects of Research" as set forth in The Belmont Report, published by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research in April 1979.

2. Like all VA employees, VHA employees conducting or reviewing research are subject to the Federal Criminal Code and the Standards of Ethical Conduct for Executive Branch Employees. The obligation to act in accordance with ethics laws and regulations applies to all individuals while acting under a VA appointment, including full and part-time employees, without compensation (WOC) employees, and employees under the Intergovernmental Personnel Act (IPA) of 1970. Ethics officials in the Office of General Counsel in VA Central Office and VA Regional Counsel Offices are available to provide guidance on dealing with actual or potential conflicts of interest. Both VA Central IRB and the {Name of Local VA Facility} will evaluate any potential conflict of interest issues of all members of the local research team in accordance with their respective policies and standard operating procedures (SOPs).

3. Both signatory institutions will adhere to 38 CFR 16 and 17, 45 CFR 46 Subpart A, and 21 CFR 50 and 56; and other pertinent VA and Federal requirements applicable to human subjects research. If the Chief Research and Development Officer (CRADO) approves research involving children or prisoners in accordance with VHA Handbook 1200.5, investigators must comply with 45 CFR 46, Subparts D or B, respectively. VA Central IRB or the {Name of Local VA Facility} will not approve a research project if it does not meet all these requirements. VHA Handbook 1200.5 will serve as the reference source for the definitions of all terms used in this MOU.

4. In accordance with the Health Insurance Portability and Accountability Act (HIPAA), 45 CFR 164.512(i), and VHA Handbook 1605.1, Privacy and Release of Information, VA Central IRB may grant a HIPAA Waiver of Authorization for use or disclosure of protected health information (PHI) for research reviewed by VA Central IRB, if justified and if all criteria for a waiver of authorization are met.

5. The VHA Central Office and the {Name of Local VA Facility} will each maintain a current Federalwide Assurance (FWA) through VA Office of Research Oversight (ORO) and the Department of Health and Human Services Office for Human Research Protections (OHRP) listing VA Central IRB as an IRB of record. The Principal Deputy Under Secretary for Health serves as the Institutional Official and the CRADO serves as the Human Protections Administrator (HPA) for the VHA Central Office Human Research Protections Program (HRPP). Any change or modification in the FWA status of either Institution will be reported to the other immediately in writing (within 1 working day).

6. Both the VHA Central Office and the {Name of Local VA Facility} will secure and maintain accreditation of their HRPPs through VA-designated accrediting organization as appropriate and per VA requirements.

7. There will be no charge to the {Name of Local VA Facility} or to investigators for the use of VA Central IRB.

RESPONSIBILITIES OF THE VHA CENTRAL OFFICE HRPP AND VA CENTRAL IRB

The VHA Central Office HRPP assures {Name of Local VA Facility} that the VHA Central Office HRPP and VA Central IRB will carry out the following functions and responsibilities in accordance with all applicable requirements:

1. The Institutional Official will ensure that VA Central IRB is provided, through the Chief Research and Development Officer (CRADO), with sufficient resources to support VA Central IRB operations. These resources will include, but not be limited to, adequate meeting space, equipment, financial support, and staff.

2. VA Central IRB will maintain current OHRP IRB registration in accordance with the requirements specified in VHA Handbook 1200.5. It will submit updates to the registration as its membership changes in accordance with the requirements in VHA Handbook 1058.03.

a. All VA Central IRB members and staff will receive appropriate initial and ongoing training with regard to VA and other Federal requirements for the protection of human subjects.

b. VA Central IRB will manage any conflicts of interest of IRB members in accordance with 38 CFR 16 and other applicable Federal and VA requirements. VA Central IRB members will recuse themselves from any discussion on any protocol or protocol-related matter in which those members have a conflict of interest. Members may provide information concerning proposals if asked by the presiding VA Central IRB Chair, but will leave the room prior to any further discussion and/or vote.

3. The VHA Central Office HRPP will maintain policies and Standard Operating Procedures (SOPs) that incorporate, whether by inclusion or reference, Federal statutes and regulations, as well as VA, VHA, and other policies, procedures, and requirements applicable to reviewing human subjects research.

a. The SOPs will include processes for compliance monitoring, audits, and reporting to appropriate regulatory authorities by VA Central IRB and its administrative staff, as well as by the participating local VA facilities as appropriate.

b. The SOPs will also include processes for reporting results of any external monitoring or audits (e.g., Food and Drug Administration (FDA), OHRP) of VA Central IRB research oversight activity that impacts the research being conducted at the {Name of Local VA Facility} to the {Name of Local VA Facility}'s Institutional Official. This includes visits by sponsors and regulatory or compliance entities.

c. All VA Central IRB SOPs will be reviewed at least annually for compliance with all pertinent VA and other Federal requirements.

4. VA Central IRB will meet a minimum of once a month, and can meet more often if determined necessary by VA Central IRB Co-Chairs and VA Central IRB administrative staff. Members will attend in-person or via audio or video conference. If the Co-Chairs and administrative staff determine there are no agenda items that require action by the convened IRB, the scheduled meeting may be cancelled.

5. VA Central IRB will perform initial review of selected multi-site research projects.

a. VA Central IRB will evaluate local context for each protocol submitted using one or more of the following methods:

i. Reviewing the {Name of Local VA Facility}'s Local Site Application (VA Central IRB Form 104), and any additional information submitted by the Local Site Investigator or the {Name of Local VA Facility}.

ii. Knowledge of the local research context by one or more of VA Central IRB members or staff. Such knowledge may have been obtained through direct experience with the {Name of Local VA Facility}, its subject populations, and/or the local community.

iii. Obtaining relevant information from an appropriate ad hoc advisor(s) who has had direct experience with the {Name of Local VA Facility}, its subject populations, and/or the local community.

iv. Systematic, reciprocal, and documented communication between VA Central IRB and {Name of Local VA Facility}. This communication will include regular interactions with one or more designated site liaisons by one or more VA Central IRB members or administrative staff and/or periodic visits to the {Name of Local VA Facility} as prescribed by VA Central IRB and {Name of Local VA Facility}'s SOPs.

b. VA Central IRB will require the use of an informed consent document for all research involving human subjects unless this requirement is waived by VA Central IRB. The informed consent document and process, waiver of documentation of informed consent, or waiver of informed consent, must meet all requirements in VHA Handbook 1200.5.

c. VA Central IRB will provide a timely written notice (usually within 10 working days of a VA Central IRB action) to the {Name of Local VA Facility} of any action requiring the {Name of Local VA Facility}'s response. Such actions

include VA Central IRB's initial review considerations and its final approval or disapproval of a project.

6. VA Central IRB will conduct meaningful and substantive continuing review of approved projects at a minimum of once per year or more often if determined appropriate to the degree of risk to subjects. The continuing review will evaluate information submitted by the Principal Investigator (PI) including, but not limited to, the continuing review application containing all the elements required by VHA Handbook 1200.5 and all interim reports.

a. VA Central IRB will remain cognizant of local issues throughout the duration of the project and may request additional information from local sources or ad hoc advisors to supplement its review.

b. VA Central IRB will provide a timely (within 10 working days), written notice of the results of the continuing review to the {Name of Local VA Facility}, including any lapses of approval, in accordance with VA Central IRB SOPs.

7. VA Central IRB will evaluate any requests to amend or modify a previously approved protocol. VA Central IRB will notify all participating local sites in writing within 10 working days after it approves any amendment or modification to a protocol. VA Central IRB will provide a copy of the approval and the amendment or modification to all participating local sites.

8. VA Central IRB oversight of approved projects will include, but not be limited to:

a. Requiring all VA Central IRB-approved projects that present greater than minimal risk to contain a specific data safety monitoring plan that includes a means of communication between the PI and local site investigators to ensure adherence to the plan.

b. Working closely with the {Name of Local VA Facility} to investigate any complaints from subjects or others, incidents of investigator noncompliance or unanticipated problems, and to coordinate required reporting to regulatory agencies in accordance with VA Central IRB SOPs, local site SOPs, and all VA and other Federal requirements.

c. Sending any of its members or administrative staff to a participating local site if determined necessary to complete any investigation or if requested by the {Name of Local VA Facility}.

9. If VA Central IRB determines that a given project does not constitute research, or does not constitute human research, it will provide a written letter with its decision to the PI who will be responsible for providing the letter to participating local VA facilities.

10. If VA Central IRB determines that a given project is exempt from IRB review, it will provide a written letter with its decision to the PI who will be responsible for providing the letter to all Local Site Investigators to share with their respective participating local VA facilities.

11. VA Central IRB will review the PI's Initial Application for each protocol to determine which sites are engaged and, therefore, require a Local Site Investigator and a Local Site Application.

12. VA Central IRB will maintain a website that will contain VA Central IRB SOPs, application forms, instructions, deadlines, reviewer checklists, a list of VA Central IRB-approved projects, local VA facilities that use VA Central IRB, and other relevant information about the VHA Central Office HRPP and VA Central IRB.

13. The VHA Central Office HRPP will seek feedback from the PI, Local Site Investigators, participating local VA facilities, and regulatory officials on the efficiency and effectiveness of VA Central IRB operations as part of the continuous quality improvement process.

14. VA Central IRB will maintain all applications, membership documents, and other relevant records in accordance with VA Central IRB SOPs, and all VA and other Federal requirements. VA Central IRB will provide {Name of Local VA Facility} ready access to pertinent VA Central IRB records for review and/or copying as needed in conjunction with any HRPP accreditation review, regulatory requirement, or in any matter concerned with the rights and welfare of any subject.

RESPONSIBILITIES OF {NAME OF LOCAL VA FACILITY}

The {Name of Local VA Facility}'s Institutional Official assures the VHA Central Office HRPP and VA Central IRB that {Name of Local VA Facility} will assume the following responsibilities in accordance with all applicable VA and other Federal requirements. {Name of Local VA Facility} will:

1. Retain ultimate responsibility for oversight of its local HRPP that includes:

a. Ensuring that all research approved or determined exempt by the VA Central IRB is submitted to the local site R&D Committee for review.

b. Safeguarding the rights and welfare of human subjects of all research approved by its R&D Committee.

c. Educating the members of its research community to establish and maintain a culture of compliance with all VA and other Federal requirements, as

well as all {Name of Local VA Facility} requirements relevant to the protection of human subjects.

d. Instituting appropriate local oversight mechanisms to ensure compliance with the determinations of VA Central IRB. This includes performing routine audits and monitoring of locally conducted VA Central IRB-approved projects and reporting results of these activities to VA Central IRB.

e. Promptly informing VA Central IRB of any complaints from subjects or others; unanticipated problems involving risks to subjects or others; serious adverse events that are unanticipated and related to the research; suspension or termination of research activities; or serious or continuing noncompliance encountered in VA human subjects research projects approved by VA Central IRB. The {Name of Local VA Facility} will work with VA Central IRB to ensure all VA and other Federal reporting requirements are met including, but not limited to, those specified in VHA Handbook 1058.1, Reporting Adverse Events in Research to the Office of Research Oversight (ORO).

2. Modify its existing FWA, through ORO per VHA Handbook 1058.03, to designate VA Central IRB as an IRB of record.

a. If the {Name of Local VA Facility} uses one or more of its local academic affiliate's IRBs as an IRB of record, the {Name of Local VA Facility} will review the relevant MOU {Name of Local VA Facility} holds with its academic affiliate and, if necessary, modify the MOU between {Name of Local VA Facility} and its academic affiliate to permit the {Name of Local VA Facility} to use VA Central IRB.

b. If the {Name of Local VA Facility} uses the services of another VA facility's R&D Committee, then {Name of Local VA Facility} will review the relevant MOU with the other VA facility and, if necessary, modify the MOU to permit {Name of Local VA Facility} to use VA Central IRB.

3. Maintain documentation that all required training, credentialing and privileging is up to date for all local HRPP staff and for all local research team members of VA Central IRB-approved projects.

4. Work with the Local Site Investigator in preparing the Local Site Application to participate in any research project that has been designated for review by VA Central IRB. The Local Site Investigator will submit the Local Site Application to the PI and VA Central IRB through the local Associate Chief of Staff (ACOS) for R&D (or equivalent).

5. Provide comments and/or suggestions to VA Central IRB about VA Central IRB's initial review considerations in a timely manner, not to exceed 30 calendar days, from the date of receipt of the initial review considerations.

6. Notify the Local Site Investigator and VA Central IRB in a timely manner, not to exceed 10 calendar days after receipt of VA Central IRB's final approval of a project, whether or not the local site chooses to participate or declines to participate in the project.

7. Ensure the project is reviewed at the next regularly scheduled meeting of its R&D Committee after it agrees to participate in a given VA Central IRB-approved project.

8. Ensure that the project is not started until it has been approved by ***both*** VA Central IRB and the local R&D Committee.

9. Forward any Freedom of Information Act (FOIA) requests received by {Name of Local VA Facility} for any records concerning VA Central IRB documents to the VHA Central Office FOIA Officer for review and release as applicable.

10. Agree not to independently modify any VA Central IRB-approved protocol except where necessary to eliminate apparent immediate hazards to the human subjects in accordance with 21 CFR 56.108(a) and 38 CFR 16.103(b)(4).

a. VA Central IRB must be notified within 5 working days if such an action is taken.

b. VA Central IRB will not review emergency use of test articles. Such use must be reviewed at the local level in accordance with the {Name of Local VA Facility}'s policies and procedures.

11. Notify VA Central IRB immediately of potential research impropriety, misconduct, suspension, debarment, or restriction of any local research team member associated with a VA Central IRB-approved project.

12. Provide VA Central IRB access to the research subjects' clinical records and/or case files if required as part of any VA Central IRB oversight or monitoring activity. This includes providing access to any VA Central IRB member, administrative staff, or designee.

13. Participate in the annual review of the VHA Central Office HRPP, including an evaluation of VA Central IRB composition and operations, in accordance with VA Central IRB SOPs and as required by VHA Handbook 1200.1, the R&D Committee Handbook.

14. Maintain compliance with any additional state, local, or institutional requirements related to the protection of human subjects. {Name of Local VA Facility} should consult its VA Regional Counsel Office or Office of General Counsel as needed.

15. Promptly notify VA Central IRB and the PI of any changes in the local study team on active projects.

16. Provide procedures for coordinating approval of local committees, including but not limited to the R&D Committee, Radiation Safety Committee, Biosafety Committee, Institutional Animal Care and Use Committee (IACUC), and/or any other relevant local committees in accordance with local SOPs. Copies of such approvals must be submitted to VA Central IRB.

17. Conduct routine compliance audits and monitoring and report findings to appropriate regulatory authorities and VA Central IRB. This includes any audits or monitoring plan included in VA Central IRB final approval of the project.

18. Maintain a file on each VA Central IRB-approved project that will include the PI's Initial Application, the {Name of Local VA Facility}'s Local Site Application, VA Central IRB-approved consent form that will be used locally, other documents associated with the initial application, VA Central IRB final approval documents, {Name of Local VA Facility} R&D Committee approvals, local audits and monitoring reports, and any subsequent correspondence, amendments, continuing review reports and approvals, and any other pertinent documents.

19. Provide information as requested to the {Name of Local VA Facility} Local Site Investigator and the project's PI as part of the continuing review process.

20. Maintain current written SOPs that incorporate {Name of Local VA Facility}'s specific responsibilities as outlined in this MOU.

21. Comply with all VA Central IRB SOPs as applicable.

22. The {Name of Local VA Facility} will not:

a. Submit a Local Site Application for a specific project to VA Central IRB if another IRB of record for {Name of Local VA Facility} has already disapproved that VA facility's participation in the project.

b. Submit an application to another IRB of record for review if VA Central IRB has determined that the {Name of Local VA Facility} should not participate in a specific project.

23. Upon approval of this agreement by both parties and the addition of VA Central IRB as an IRB of record on the {Name of Local VA Facility}'s FWA, the {Name of Local VA Facility}'s Institutional Official will provide a letter to VA Central IRB designating in writing which local official (e.g., Associate Chief of Staff for Research and Development (ACOS for R&D), Administrative Officer for R&D, R&D Committee Chair, local IRB Chair) is authorized to perform each of

the following three functions on behalf of {Name of Local VA Facility} (NOTE: One local official may have authority to perform all three functions, or each of the functions may be delegated to different local officials). The appointment letter must also include the names and contact information for each designated local official, including what function each official is performing if more than one is appointed.

a. Providing comments and/or suggestions to VA Central IRB in response to VA Central IRB initial review considerations.

b. Responding to VA Central IRB's final approval of the project on behalf of {Name of Local VA Facility} as to whether the {Name of Local VA Facility} chooses to participate or declines to participate in the project.

c. Serving as the liaison among VA Central IRB, the Local Site Investigator, and the {Name of Local VA Facility} for oversight, compliance, and monitoring purposes.

TERMINATION PROVISIONS

1. This MOU may be terminated by either the {Name of Local VA Facility} or the VHA Central Office HRPP without cause by giving a 60 day advance written notice of termination to the other Institution and to ORO. The 60 day notice period will not start until receipt of the written notice by the other party. The agreement may be terminated for cause only under the direction and guidance of ORO.

2. All current and active protocols will continue to be monitored under the provisions of the agreement until all VA Central IRB-approved projects active at the {Name of Local VA Facility} have been closed or safely moved to another site. The {Name of Local VA Facility} will maintain all documentation regarding the site's participation in the project in accordance with the time frames specified in VA and other Federal requirements.

3. This agreement will go into effect the date of signature by the VHA Central Office Institutional Official and will remain in effect until terminated as above or the agreement is amended and/or revised per mutual agreement of both Institutions. As required by VHA Handbook 1058.03, this agreement will be reviewed every 3 years by each institution at the time of renewal of that institution's FWA to determine if any conditions have changed that will require revision of the agreement.

_____ Signature of Local VA Facility Director	_____ Signature of Network Director
Name of Local VA Facility Local VA Facility Address	Network Name Network Address
Date:_____	Date: _____

_____
Joel Kupersmith, MD
Chief Research and Development Officer on behalf of VHA Central Office HRPP Institutional Official

Office of Research and Development (12)
810 Vermont Avenue, NW
Washington, DC 20420

Date: _____